DETAILED ACTION

Status of Claims

1. Claims 23, 26, 96 and 99 are cancelled. Claims 1-22, 24-25 and 27-95, 97-98, 100-147 are pending. Claims 28-66 and 101-139 are withdrawn from examination because the claims are directed to a non-elected invention. Claims 1-22, 24-25, 27, 67-95, 97-98, 100 and 140-147 are under examination.

2. Additionally, to allow the entry of the rejection(s) provided herein, the office action is non-final. The Office truly regrets the inconvenience this may cause Applicant.

Claim Rejections - 35 USC § 102

3. The anticipatory rejection is withdrawn in view of Applicant's submission.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The rejection of the claims as being obvious over Ramshaw et al. and Hoo, separately, is withdrawn in view of Applicant's submission.

6. Claims 1-22, 24-25, 27, 69-73, 74-95, 97-98, 100 and 142-147 are rejected under 35 U.S.C. 103(a) as being unpatentable over Babai et al.[1] in view of Faulkner et al.,[2] as evidenced by Masuda et al.[3]

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[1] Babai et al. A novel liposomal influenza vaccine (INFLUSOME-VAC) containing hemagglutinin–neuraminidase and IL-2 or GM-CSF induces protective anti-neuraminidase antibodies cross-reacting with

The claims are directed to a cell comprising a vector and a vector comprising a nucleic acid molecule encoding a fusion polypeptide comprising i) a first amino acid sequence that can bind to a carbohydrate on a glycoprotein, wherein the carbohydrate is a sialic acid; and ii) a second amino acid sequence comprising the sequence of a ligand for a cell surface polypeptide, wherein the ligand is a ligand for a cytokine receptor. Claims 2-3, which depend on claim 1, require the first amino acid sequence to be N-terminal and C-terminal to the second amino acid sequence, respectively. Claim 4, which depends on claim 1, requires the sialic acid to comprise one of the following structures: N-acetylneuraminic acid, alpha-NeuNAc-[2->6]-Gal, alpha-NeuNAc-[2->6]-GalNAc, alpha-NeuNAc-[2->3]-Gal. Claim 5, which depends on claim 1, requires the first amino acid sequence to comprise a carbohydrate-binding domain of a naturally occurring lectin. Claim 6, which depends on claim 1, requires the first amino acid sequence to comprise at least 10 contiguous amino acids of a hemagglutinin, which is limited to an influenza virus hemagglutinin by claim 7, which is further limited to the HA1 domain of the influenza virus hemagglutinin by claim 8. Claim 9, which depends on claim 7, limits the influenza virus to influenza A virus, which is further limited to an H1 subtype by claim 11, which is further limited to the A/PR/8/34 strain by claim 12. Claim 10, which depends on claim 9, limits the influenza virus to a subtype that infects humans, which is limited to the H2 or H3 subtype. Claim 14, which depends on claim 7,

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a wide spectrum of influenza A viral strains. Vaccine, Volume 20, Issues 3-4, 12 November 2001, Pages 505-515

[2] Faulkner et al. Influenza hemagglutinin peptides fused to interferon gamma and encapsulated in liposomes protects mice against influenza infection. Vaccine, February 14, 2003, Vol. 21, 932-939.

[3] Masuda et al. Substitution of amino acid residue in influenza A virus hemagglutinin affects recognition of sialyl-oligosaccharides containing N-glycolylneuraminic acid. FEBS Letters, 1999, Vol. 464, 71-74.

requires the virus be of a subtype that does not infect humans. Claim 15, which depends on claim 1, limits the ligand for a cell surface polypeptide to a ligand for a mammalian cell surface polypeptide. Claims 16-17, which depend on claim 15, limit the mammalian cell surface polypeptide to mouse and human cell surface polypeptide, respectively. Claim 18, which depends on claim 1, limits the ligand for a cell surface polypeptide to a ligand for a cell surface polypeptide of a leukocyte, which is further limited to dendritic cells by claim 21. Claim 19, which depends on claim 1, limits the ligand for a cell surface polypeptide be a ligand for a cell surface polypeptide of an antigen presenting cell, which is further limited to a professional antigen presenting cell by claim 20. Claims 22 and 24, which depend on claim 1, limit the ligand for a cell surface polypeptide to a ligand for a mouse GM-CSF receptor and to comprise a mouse GM-CSF receptor, respectively. Claims 25 and 27, which depend on claim 1, limit the ligand for a cell surface polypeptide to a ligand for a human GM-CSF receptor and to comprise a human GM-CSF receptor, respectively. Claim 69, which depends on claim 1, requires the fusion polypeptide to comprise a secretory signal sequence. Claim 70, which depends on claim 1, requires the expression vector to be a eukaryotic expression vector, which is limited to a yeast and mammalian expression vector by claims 71-72. Claim 73, which depends on claim 1, requires the vector to comprise an inducible promoter. Claims 74-95, 97-98, 100 and 142 is directed to a cell comprising the vector described above. Claim 143, which depends on claim 74, requires the cell to be prokaryotic. Claim 144, which depends on claim 74, requires the cell to be eukaryotic,

which is later limited to yeast, mammalian and insect cells by claims 145-147, respectively.

Babai et al. teaches a composition comprising two amino acid sequences. The first amino acid sequence is that of the influenza hemagglutinin. The second amino acid sequence is that of GM-CSF. The influenza hemagglutinin used by Babai et al. is derived from influenza A/Shangdong/9/93, which is H3N2 subtype that infects humans. Hemagglutinin (HA) is a lectin, which has a carbohydrate-binding domain. HA is also binds to sialic acid, as evidenced by Masuda et al. Masuda et al. also evidences that sialic acid derivatives include the following structures: N-acetylneuraminic acid, alpha-NeuNAc-[2->6]-Gal, alpha-NeuNAc-[2->6]-GalNAc and alpha-NeuNAc-[2->3]-Gal. In the instant case, Babai et al. used the entire HA protein, which comprises at least 10 contiguous amino acids and includes the HA1 portion. The GM-CSF used by Babai et al. is a ligand for a mammalian cell surface polypeptide, particularly that of mouse. Specifically, the ligand is a ligand for a cell surface polypeptide of a leukocyte, specifically dendritic cells, which is a professional antigen presenting cell. In the instant case, because Babai et al. used the entire GM-CSF sequence, Babai et al. used at least 5 contiguous amino acids of a the mouse GM-CSF.

The difference between the claimed invention and the invention is: Babai et al. did not fuse the two amino acid sequences. However, the deficiency noted in Babai et al. is fully compensated by Faulkner et al. Additionally, Faulkner et al. teaches a vector comprising a nucleic acid molecule encoding for the fusion polypeptide; and a cell comprising the vector. The fusion polypeptide of Faulkner et al. comprises a secretory

signal sequence; and the vector comprises an inducible promoter. The cell used by Faulkner et al. is a prokaryotic cell.

Faulkner et al. teaches that the immunogenicity of a peptide vaccine may be improved by fusing antigen and cytokine. In the instant case, the HA used by Babai et al. is an antigen and GM-CSF is a cytokine. Hence, at the time the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to fuse the HA antigen of Babai et al. with GM-CMSF. One of ordinary skill in the art, at the time the invention was made would have been motivated to do so to improve the immunogenicity of the vaccine made by Babai et al. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because Faulkner et al. demonstrated fusion improved immunogenicity.

It would also been prima facie obvious for one of ordinary skill in the art to obtain the nucleic acid sequence of the fusion polypeptide rendered obvious by Faulkner et al. and Babai et al. and insert it into an expression vector, including eukaryotic vector systems such as mammalian and yeast expression vectors with an inducible promoter, and transfect cells, including prokaryotic and eukaryotic cells such as mammalian, yeast and insect cells with the expression vector. One of ordinary skill in the art, at the time the invention was made would have been motivated to do so to express the fusion polypeptide rendered obvious by Babai et al. and Faulkner et al. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because the use of expression vectors and transfection of cells with said vectors are routinely practiced in the art. See MPEP 2143.01, *Ex parte Kubin*.

While it is not readily apparent if Faulkner et al. fused the antigen to the N or C terminal of the cytokine, however, it is noted that there exist 2 fusion sites, either the N or the C terminal. Thus, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to fuse the HA antigen of Babai et al. to either the N or the C terminal of GM-CSF. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to fuse the antigen and cytokine. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because there are a finite number of fusion sites.

It is noted that some of the claims requires the use of a human GM-CSF. In the instant case, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to substitute the mouse GM-CSF used by Babai et al. to that of a human GM-CSF. One of ordinary skill in the art, at the invention was made, would have been motivated to do so to make a fusion composition that is suitable for human use. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the substitution of known/functional alternatives is routinely practiced in the art.

Additionally, while the subtype used by Babai et al. is not an H1 subtype or is the A/PR/8/34; however, at the time the invention was made, this subtype and strain has been well characterized, as evidenced by the disclosure of Masuda et al. Thus, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to substitute the HA antigen of Babai et al. to that of the HA

antigen derived from A/PR/8/34 strain, which is an H1 subtype. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to make a composition that is specific for the particular A/PR/8/34 strain. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the substitution of known/functional alternatives is routinely practiced in the art.

7. Claims 1, 67-68 and 140-141 are rejected under 35 U.S.C. 103(a) as being unpatentable over Babai et al. in view of Faulkner et al., as evidenced by Masuda et al., as applied to claim 1, in further view of Shao et al.[4]

Claim 67, which depends on claim 1, requires that a linker interposed between the first and second amino acid sequences. Claim 68, which depends on claim 67, requires the linker to be $(Gly_xSer)_n$, wherein n is between 1-15 and x is between 1-10. Claims 140-141 are directed to the same limitation as described in claims 67-68 for a cell.

The significance of Babai et al., Faulkner et al. and Masuda et al., as applied to claim 1 is provided above.

Babai et al., Faulkner et al. and Masuda et al. do not teach the use of a linker. However, Shao et al. teaches the use of a linker to minimize steric hinderance between two sequences. The linker used by Shao et al. is $(GlySer)_5$. Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to use $(GlySer)_5$ as a linker interposing between the HA antigen and GM-CSF of

Babai et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do to minimize any steric hinderance posed by linking HA with GM-CSF. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the use of linkers is routinely practiced in the art.

Conclusion

8. No claims are allowed. As noted above, to allow the entry of the rejection(s) set herein, the office action is non-final.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571)272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

[4] Shao et al. Anchor-Chain Molecular System for Orientation Control in Enzyme Immobilization. Bioconjug., Chem., 2000, Vol. 11: 822-826.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Emily Le/
Primary Examiner, Art Unit 1648

/E. L./